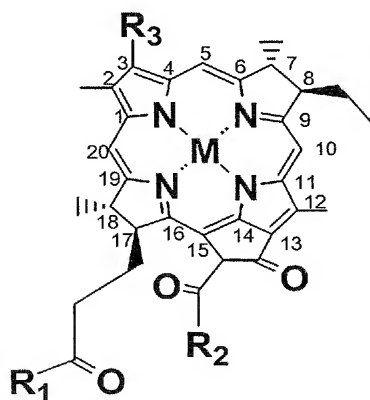


AMENDMENTS TO THE CLAIMS:

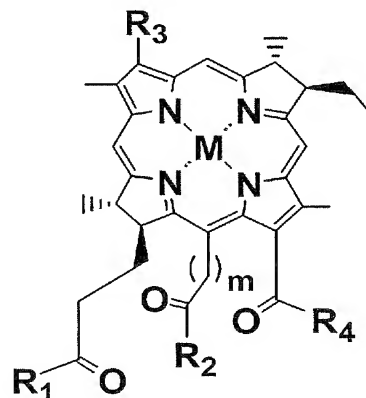
This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A bacteriochlorophyll ~~derivative compound~~ containing at least one, ~~preferably two or three,~~ negatively charged ~~groups-group~~ or acidic ~~groups-group~~ that ~~are~~ is converted to negatively charged groups at the physiological pH, of the formula I or II:



(I)



(II)

wherein

M represents 2H or a metal atom selected from the group consisting of divalent Pd, Pt, Co, Sn, Ni, Cu, Zn and Mn, or trivalent Fe, Mn and Cr;

R₁, R₂, and R₄ each independently is Y- R₅;

Y is O, S or -NR₆;

R₃ is selected from the group consisting of -CH=CH₂, -C(=O)-CH₃, -C(=O)-H, -CH=NR₇, -C(CH₃)=NR₇, -CH₂-OR₇, -CH₂-SR₇, -CH₂-NR₇R'₇, -CH(CH₃)-OR₇, -CH(CH₃)-SR₇, -CH(CH₃)-NR₇R'₇, -CH(CH₃)Hal, -CH₂-Hal, -CH₂-R₇, -CH=CR₇R'₇, -C(CH₃)=CR₇R'₇, -CH=CR₇Hal, -C(CH₃)=CR₇Hal, and -C≡CR₇;

R₅, R₆, R₇ and R'₇ each independently is H or selected from the group consisting of:

(a) C₁-C₂₅ hydrocarbyl optionally containing one or more heteroatoms selected from the group consisting of -O, S and N, carbocyclic or heterocyclic moieties such as pyridyl, and/or optionally substituted by one or more functional groups selected from the group consisting of halogen, oxo, OH, SH, CHO, NH₂, CONH₂, a negatively charged group, and an acidic group that is converted to a negatively charged group at the physiological pH;

(b) a residue of an amino acid, a peptide or of a protein;
and

(c) when Y is O or S, R₅ may further be R₈⁺;

m is 0 or 1; and

R₈⁺ is H⁺ or a cation;

provided that:

(i) at least one of R₅, R₆, R₇ and R'₇ is a hydrocarbon chain as defined in (a) above substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH; or

(ii) at least one of R_1 , R_2 , and R_4 is OH, SH, $O^-R_8^+$ or $S^-R_8^+$; or

(iii) at least one of R_1 , R_2 , and R_4 is OH, SH, $O^-R_8^+$ or $S^-R_8^+$ and at least one of R_5 , R_6 , R_7 and R'_7 is a hydrocarbon chain substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH; or

(iv) at least one of R_1 , R_2 , and R_4 is OH, SH, $O^-R_8^+$ or $S^-R_8^+$ and at least one of R_5 , R_6 , R_7 and R'_7 is a residue of an amino acid, a peptide or of a protein; or

(v) at least one of R_5 , R_6 , R_7 and R'_7 is a hydrocarbon chain substituted by a negatively charged group or by an acidic group that is converted to a negatively charged group at the physiological pH and at least one of R_5 , R_6 , R_7 and R'_7 is a residue of an amino acid, a peptide or of a protein;

wherein said negatively charged group is selected from the group consisting of COO^- , COS^- , SO_3^- , and PO_3^{2-} and said acidic group that is converted to a negatively charged group at the physiological pH is selected from the group consisting of COOH, COSH, SO_3H , and PO_3H_2 ;

but excluding the compounds of formula I wherein M is as defined, R_3 is $-C(=O)CH_3$, R_1 is OH or OR_8^+ and R_2 is $-OCH_3$, and the compound of formula II wherein M is 2H, R_3 is $-C(=O)CH_3$, R_1 , R_2 and R_4 are OH, and m is 0 or 1. ~~or both, excluding pentacyclie~~

~~bacteriochlorophyll derivatives having a free $\text{CH}_2\text{CH}_2\text{COOH}$ or a $\text{CH}_2\text{CH}_2\text{COO}^-$ group at position 17, and tetraacyelic bacteriochlorophyll derivatives devoid of a central metal atom and having a $\text{CH}_2\text{CH}_2\text{COOH}$ group at position 17, a CH_2COOH or COOH group at position 15, a COOH group at position 13, methyl groups at the positions 2, 7, 12, 18, and ethyl groups at the positions 3 and 8.~~

2. (Currently Amended) A The bacteriochlorophyll derivative compound according to claim 1 containing two negatively charged groups.

3. (Currently Amended) A The bacteriochlorophyll derivative compound according to claim 1 containing three negatively charged groups.

4-9. (Cancelled)

10. (Currently Amended) A The bacteriochlorophyll derivative compound of the formula I or II according to claim 7-1, wherein R_1 is $\text{Y}-\text{R}_5$; Y is O, S or NH; and R_5 is a hydrocarbon chain substituted by functional groups selected from of the group consisting of OH, SH, SO_3H , NH_2 , CONH_2 , COOH , COSH , and PO_3H_2 .

11. (Currently Amended) A The bacteriochlorophyll derivative compound of the formula I or II according to claim 7 1, wherein R_5 is the residue of an amino acid, a peptide or a protein.

12. (Currently Amended) A The bacteriochlorophyll derivative compound of the formula I or II according to claim 7 1 containing a central Pd metal atom.

13. (Currently Amended) A The bacteriochlorophyll derivative compound of the formula I according to claim 7 1, wherein:

M is Pd;

R_1 is $-\text{NH}-(\text{CH}_2)_n-\text{SO}_3^-\text{R}_8^+$, $-\text{NH}-(\text{CH}_2)_n-\text{COO}^-\text{R}_8^+$; $-\text{NH}-(\text{CH}_2)_n-\text{PO}_3^{2-}(\text{R}_8^+)_2$;

R_2 is methoxy;

R_3 is $-\text{C}(=\text{O})-\text{CH}_3$;

R_8^+ is a monovalent cation such as K^+ , Na^+ , Li^+ , NH_4^+ ; and

n is an integer from 1 to 10, ~~preferably 2 or 3.~~

14. (Currently Amended) A The bacteriochlorophyll derivative compound of the formula II according to claim 7 1, wherein:

M represents 2H, divalent Pd, Cu, or Zn or trivalent Mn;

Appln. No. 10/534,692
Amdt. dated January 25, 2010
Reply to Office Action of September 24, 2009

R_1 is $-O^-R_8^+$, $-NH-(CH_2)_n-SO_3^-R_8^+$, $-NH-(CH_2)_n-COO^-R_8^+$ or $-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$; or $Y-R_5$, wherein Y is O, S or NH and R_5 is the residue of an amino acid, a peptide or a protein;

R_2 is C_1-C_6 alkoxy, ~~preferably methoxy~~;

R_3 is $-C(=O)-CH_3$, $-CH=N-(CH_2)_n-SO_3^-R_8^+$; $-CH=N-(CH_2)_n-COO^-R_8^+$; $-CH=N-(CH_2)_n-PO_3^{2-}(R_8^+)_2$; $-CH_2-NH-(CH_2)_n-SO_3^-R_8^+$; $-CH_2-NH-(CH_2)_n-COO^-R_8^+$; or $-CH_2-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$;

R_4 is $-NH-(CH_2)_n-SO_3^-R_8^+$; $-NH-(CH_2)_n-COO^-R_8^+$; or $-NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$;

R_8^+ is a monovalent cation, ~~preferably K^+~~ ; and

m is 1, and n is an integer from 1 to 10, ~~preferably 2 or 3~~.

15. (Currently Amended) ~~A~~ The bacteriochlorophyll
derivative compound of formula II in claim 7 1 wherein:

M is divalent Pd;

R_1 is $-O^-R_8^+$, $-NH-(CH_2)_n-SO_3^-R_8^+$, or $Y-R_5$, wherein Y is O, S or NH and R_5 is the residue of an amino acid, a peptide or a protein;

R_2 is C_1-C_6 alkoxy, ~~preferably methoxy~~;

R_3 is $-C(=O)-CH_3$, $-CH=N-(CH_2)_n-SO_3^-R_8^+$; or $-CH_2-NH-(CH_2)_n-SO_3^-R_8^+$;

R_4 is $-NH-(CH_2)_n-SO_3^-R_8^+$; $NH-(CH_2)_n-COO^-R_8^+$; or $NH-(CH_2)_n-PO_3^{2-}(R_8^+)_2$;

R_8^+ is a monovalent cation, ~~preferably K^+~~ ;

m is 1, and n is 2 or 3.

16. (Currently Amended) ~~A~~-The bacteriochlorophyll derivative compound of the formula I according to claim 13, consisting of the compound Palladium bacteriopheophorbide a 17³-(3-sulfopropyl)amide potassium salt.

17. (Currently Amended) ~~A~~-The bacteriochlorophyll derivative compound of the formula II according to claim 15, selected from the group consisting of:

Palladium 3¹-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13¹-(2-sulfoethyl) amide dipotassium salt;

3¹-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13¹-(2-sulfoethyl) amide dipotassium salt;

Palladium 3¹-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13¹,17³-di(3-sulfopropyl)amide dipotassium salt;

Palladium 3¹-(3-sulfopropylimino)-15-methoxycarbonylmethyl-rhodobacterio-chlorin 13¹,17³-di(3-sulfopropyl)amide tripotassium salt;

Copper(II) 3¹-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13¹-(2-sulfoethyl) amide dipotassium salt;

Zinc 3¹-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13¹-(2-sulfoethyl) amide dipotassium salt;

Appln. No. 10/534,692
Amdt. dated January 25, 2010
Reply to Office Action of September 24, 2009

Manganese(III) 3¹-oxo-15-methoxycarbonylmethyl-
rhodobacteriochlorin 13¹-(2-sulfoethyl)amide dipotassium salt;

Palladium 3¹-oxo-15-methoxycarbonylmethyl-
rhodobacteriochlorin 13¹-(2-sulfoethyl) amide, 17³-(N-
immunoglobulin G) amide potassium salt;

Palladium 3¹-oxo-15-methoxycarbonylmethyl-
rhodobacteriochlorin 13¹-(2-carboxy-ethyl)amide dipotassium salt;

Palladium 3¹-oxo-15-methoxycarbonylmethyl-
rhodobacteriochlorin 13¹-(3-phosphopropyl)amide tripotassium
salt; and

Palladium 3¹-(3-sulfopropylamino)-15-methoxycarbonylmethyl-
rhodobacte-riochlorin 13¹,17³-di(3-sulfopropyl)amide tripotassium
salt.

18. (Original) Palladium 3¹-oxo-15-
methoxycarbonylmethyl-rhodobacteriochlorin 13¹-(2-sulfoethyl)
amide dipotassium salt.

19. (Currently Amended) A pharmaceutical composition
comprising a the bacteriochlorophyll derivative compound according
to claim 1, and a pharmaceutically acceptable carrier.

20-35. (Cancelled)

36. (Currently Amended) A method for vascular-targeted
~~tumor~~ photodynamic therapy (VTP), which comprises:

- (a) administering to an individual in need a the
bacteriochlorophyll compound according to claim 1; and
- (b) irradiating the local area of the tumor.

37. (Currently Amended) A method for photodynamic
therapy of age-related macular degeneration by vascular
occlusion, which comprises:

- (a) administering to an individual in need a the
bacteriochlorophyll compound according to claim 1; and
- (b) irradiating the local area of the macular degeneration.

38. (Currently Amended) A method for tumor diagnosis
which comprises:

- (a) administering to a subject suspected of having a tumor,
a the bacteriochlorophyll compound according to claim 1; and
- (b) irradiating the subject by standard procedures and
measuring the fluorescence of the suspected area, wherein a
higher fluorescence indicates tumor sites.

39-41 (Cancelled).

42. (Currently Amended) ~~The A~~ compound Palladium bacteriopheophorbide a 17³-(3-sulfo-1-oxysuccinimide) ester sodium salt,~~as an intermediate.~~

43. (Currently Amended) A method for the preparation of compounds of formula II ~~in~~ of claim 7 1, wherein R₁ is -O⁻ R₈⁺; R₂ is -OCH₃; R₃ is acetyl; R₄ is a group -NH-(CH₂)_n-SO₃⁻ R₈⁺; R₈⁺ is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide of formula I, wherein R₁ is OH with an aminosulfonic acid of the formula H₂N-(CH₂)_n-SO₃H in a R₈⁺-buffer; and

(ii) isolating the desired compound of formula II.

44. (Currently Amended) The method according to claim 43 for preparation of palladium 3¹-oxo-15-methoxycarbonylmethyl-rhodobacteriochlorin 13¹-(2-sulfoethyl) amide dipotassium salt, which comprises: (i) reacting Pd-bacteriopheophorbide a with taurine of the formula H₂N-(CH₂)₂-SO₃H in a K⁺ -buffer; and (ii) isolating the ~~title~~ compound.

45. (Currently Amended) A method for the preparation of compounds of formula II in claim 7 1, wherein R₁ is -O⁻ R₈⁺; R₂ is -OCH₃; R₃ is acetyl; R₄ is a group -NH-(CH₂)_n-COO⁻ R₈⁺; R₈⁺ is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

Appln. No. 10/534,692
Amdt. dated January 25, 2010
Reply to Office Action of September 24, 2009

(i) reacting the corresponding M-bacteriopheophorbide of formula I wherein R_1 is OH with an aminocarboxylic acid of the formula $H_2N-(CH_2)_n-COOH$ in a R_8^+ -buffer; and

(ii) isolating the desired compound of formula II.

46. (Currently Amended) A method for the preparation of compounds of formula II in claim 7 1, wherein R_1 is $-O^- R_8^+$; R_2 is $-OCH_3$; R_3 is acetyl; R_4 is a group $-NH-(CH_2)_n-PO_3^{2-} (R_8^+)_2$; R_8^+ is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide of formula I wherein R_1 is OH with an aminophosphonic acid of the formula $H_2N-(CH_2)_n-PO_3H_2$ in a R_8 -buffer; and

(ii) isolating the desired compound of formula II.

47. (Currently Amended) A method for the preparation of compounds of formula II in claim 7 1, wherein R_1 and R_4 contain the same negatively charged group, which comprises:

(i) reacting the corresponding M-bacteriopheophorbide with an excess of the aminosulfonic, aminocarboxylic or aminophosphonic acid in a R_8^+ -buffer; and

(ii) isolating the desired 13,17-disubstituted derivative compound of formula II.

48. (Currently Amended) A method for the preparation of compounds of formula II in claim 7 1, wherein R_1 and R_4 are each a group $-\text{NH}-(\text{CH}_2)_n-\text{SO}_3^-\text{R}_8^+$; R_2 is $-\text{OCH}_3$; R_3 is acetyl; R_8^+ is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein R_1 is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17³-N-hydroxy-sulfosuccinimide ester with an excess of an aminosulfonic acid of the formula $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{SO}_3\text{H}$ in a R_8^+ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

(iii) reacting the product of step (ii) with an excess of $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{SO}_3\text{H}$ in a R_8^+ -buffer; and

(iv) isolating the desired compound of formula II.

49. (Currently Amended) A method for the preparation of compounds of formula II in claim 7 1, wherein R_1 and R_4 are each a group $-\text{NH}-(\text{CH}_2)_n-\text{COO}^-\text{R}_8^+$; R_2 is $-\text{OCH}_3$; R_3 is acetyl; R_8^+ is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein R_1 is OH with N-hydroxy-sulfosuccinimide (sulfo

NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17³-N-hydroxy-sulfosuccinimide ester with an excess of an aminocarboxylic acid of the formula $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$ in a R_8^+ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

(iii) reacting the product of step (ii) with an excess of $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{COOH}$ in a R_8^+ -buffer; and (iv) isolating the desired compound of formula II.

50. (Currently Amended) A method for the preparation of compounds of formula II in claim 7 1, wherein R_1 and R_4 are each a group $-\text{NH}-(\text{CH}_2)_n-\text{PO}_3^{2-} \text{R}_8^+$; R_2 is $-\text{OCH}_3$; R_3 is acetyl; R_8^+ is a monovalent cation; m is 1 and n is 1 to 10, which comprises:

(i) coupling the corresponding M-bacteriopheophorbide of formula I wherein R_1 is OH with N-hydroxy-sulfosuccinimide (sulfo NHS) in the presence of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC);

(ii) reacting the resulting M-bacteriopheophorbide-17³-N-hydroxy-sulfosuccinimide ester with an excess of an aminophosphonic acid of the formula $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{PO}_3\text{H}_2$ in a R_8^+ -buffer, thus obtaining a compound of formula I having a sole negatively charged group at position 17;

Appln. No. 10/534,692

Amdt. dated January 25, 2010

Reply to Office Action of September 24, 2009

(iii) reacting the product of step (ii) with an excess of $\text{H}_2\text{N}-(\text{CH}_2)_n-\text{PO}_3\text{H}_2$ in a R_8^+ -buffer; and (iv) isolating the desired compound of formula II.